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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/050,249	03/30/1998	HARUKI OKAMURA	OKAMURA=2B	6601

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EXAMINER
JIANG, DONG

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 10/21/2002

29

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/050,249	OKAMURA ET AL.	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *93-119* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *93-119* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED OFFICE ACTION

The request filed on 8 August 2002, paper No. 28, for a Continued Examination (RCE) under 37 CFR 1.114 based on parent Application No. 09/050,249 is acceptable, and a RCE has been established. An action on the RCE follows.

Applicant's amendment in paper No. 26, filed on 11 July 2002 is acknowledged and entered. Following the amendment, claim 93 is amended.

Currently claims 93-119 are pending and under consideration.

Objections and Rejections under 35 U.S.C. 112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 93-119 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons set forth in the previous Office Actions, paper No. 22, at page 3, and paper No. 24, at pages 2-3.

Claim 93 remains indefinite for reciting the term "substantially the same" physicochemical properties of (1) to (3). Applicants argument filed on 11 July 2002 (paper No. 26) has been fully considered, but are not deemed persuasive for reasons below.

At page 3 of the response, the applicant argues that the amendment of "properties of (1) to (3)" obviates the rejection, as these properties do not include an amino acid sequence. This argument is not persuasive because the claim limitation is directed to a specific protein product, which has properties described by precise structural and physicochemical parameters, such as the amino acid sequence, pI value, and the biological activity of inducing IFN-γ production. It is unclear to a person of skill in the art to define such properties using relative terms such as "substantially the same". For example, it is unclear what is intended by "substantially the same" to the part (3) of the claim, which is the biological activity of inducing IFN-γ production, and the

question raises: does the claimed protein or does not it induce IFN-γ production? Additionally, it is unclear how close to the given pI value is "substantially the same". Further, given the fact that the variant in part (ii) of the newly amended claim no longer requires the sequence identity (in part (4) of the claim), using a relative term such as "substantially the same" makes the claim even more ambiguous, as all it requires is to have "substantially the same" physicochemical properties of (1) to (3). As such, the metes and bounds of the claim cannot be determined. The claim is further indefinite because it is unclear what it is meant by the new amendment of "partial amino acid sequence possessing the amino acid sequence of SEQ ID NO:2" in part (4) of the claim, whether the term "possessing" means "comprising, and how a partial sequence comprises the whole sequence of SEQ ID NO:2.

Claim 94 remains indefinite for omitting essential elements. Applicants argument filed in paper No. 26 has been fully considered, but are not deemed persuasive for reasons below.

At page 3 of the response, the applicant argues that when the temperature is not specifically disclosed, it is understood that the temperature is ambient. This argument is not persuasive because there is no such universal rule in the art, and when it comes to hybridization conditions, the washing temperature is absolutely critical as to the removal of nonspecific hybridization complexes, and therefore, should always be specified.

The remaining claims remain rejected for depending from an indefinite claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 93, 94, 96, 118, and the dependent claims 95, 98-117 remain rejected under 35 U.S.C. 112, first paragraph, as enablement is not be commensurate in scope with the claims, for the reasons set forth in the previous Office Actions, paper No. 22, at page 4, and paper No. 24, at page 3.

Applicants argument in paper No. 26 has been fully considered, but are not deemed persuasive for reasons below.

At pages 4-5 of the response, the applicant argues that "variants of SEQ ID NO:2" are defined in claim 93, that it should be easy for a skilled artisan to obtain "variants of SEQ ID NO:2", and a monoclonal antibodies thereto, even if the specification does not disclose concrete examples, and that a skilled artisan would readily understand that such antibody has the same use as antibodies against the protein of SEQ ID NO:2. This argument is not persuasive because, as explained in the previous Office Actions, the issue is not whether a skilled artisan knows how to obtain "variants of SEQ ID NO:2", and a monoclonal antibodies thereto, and how to use such SEQ ID NO:2 specific antibodies, rather, the issue is that *the claims encompass* antibodies that bind to epitopes of the variants, which are not found in the particularly disclosed sequence, SEQ ID NO:2, and there is no written description of those epitopes. Therefore, the structural properties and use of the corresponding antibodies are not predictable. Absent a disclosed use of those antibodies non-specific to SEQ ID NO:2, the specification fails to enable the skilled artisan to make or use the *full scope* of the subject matter of the noted claims.

Claims 93-96 and 98-118 remain rejected under 35 U.S.C. 112, first paragraph, as lacking adequate written description for the variants of SEQ ID NO:2, for the reasons set forth in the previous Office Actions, paper No. 22, at page 5, and paper No. 24, at pages 4-5.

Applicants argument in paper No. 26 has been fully considered, but are not deemed persuasive for reasons below.

At page 5 of the response, the applicant argues that it would be expected by a skilled artisan that mammals other than mice would have the same or similar IFN-γ inducing substance as that of mice in the present invention, and that the present invention is a pioneer invention with regard to IFN-γ inducing substance, thus that "IGIF is obtainable from a mammal" in claim 95 should be acknowledged. This argument is not persuasive because IGIF or IL-18 is not a first invention with regard to IFN-γ inducing substance. For example, IL-12 was discovered prior to the present invention, and it is an IFN-γ inducing substance. Further, while the same or similar IFN-γ inducing substance may exist in other claimed species, the broad genus claim is represented by *one* molecular species described with particularity in the disclosure, and no other species meeting the limitations of the claim is identified or particularly described. There is no

evidence demonstrating the degree of structural or functional similarity or dissimilarity of IL-18 among species. With the exception of SEQ ID NO: 2, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. The Examiner, therefore, concludes that the one species of IL-18 is not likely to be representative of all species recited in claim 95, and thus that the disclosure does not convey to those skilled in the art that the inventors were in possession of the genus of all IL-18 at the time the application was filed.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polypeptide comprising the amino acid sequence set forth in SEQ ID NO:2, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Rejections Over Prior Art:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a

later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 93-119 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Nakamura *et al.* (*Infect. Immun.* 61: 64-70, 1993), for the reasons set forth in the previous Office Actions, paper No. 22, at pages 6-8, and paper No. 24, at pages 5-6.

Applicants argument in paper No. 26 has been fully considered, but are not deemed persuasive for reasons below.

At page 6 of the response, the applicant argues that Okamura never states that IGIF of 18-19 kDa and the factor of 75 kDa disclosed by Nakamura are the same, instead, Okamura states that IGIF of 18-19 kDa is contained in the factor of Nakamura. The applicant further argues that it is apparent that the factor of Nakamura is a mixture of IGIF and other substances, and that it would have been difficult even for one of skill in the art to recognize and successfully separate IGIF based on Nakamura's teaching, therefore, the present invention cannot be made obvious over Nakamura. This argument is not persuasive because Nakamura's factor of 75 kDa is a mixture of IGIF and other substances as demonstrated by Okamura that the molecular mass of 75 kDa IGIF was reduced to 19 kDa on 0.1% SDS-PAGE in the presence of DTT, and the N-terminal amino acid sequence is the same as that of IGIF from the liver, and that "thus IGIF in the serum sample was proved to be *the same* IGIF as that found in the liver exact "(the abstract, and page 3969, the second paragraph of the left column). Further, ever if the factor of Nakamura were a mixture of IGIF and other substances, 19 kDa IGIF is at the least a significant component thereof. As such, a significant number of the antibodies within the genus conceded to be obvious in view of it would have recognized epitopes on the 19 kDa component, and such antibodies are obvious over the present claims regardless whether the IGIF of 18-19 kDa is separated.

At page 7 of the response, applicant argues that Nakamura teaches that treatment with 2-mercaptoethanol (2-ME) resulted in augmented ability to induce IFN-γ, and that IGIF protein of the present invention is clearly distinguished from the factor of Nakamura in IFN-γ inducing activity after SDS-PAGE, and is therefore unobvious over Nakamura. This argument is not persuasive because, while the Examiner acknowledges Nakamura's teaching regard to 2-ME

treatment, the present specification does not teach that the protein used in the assays for biological activity is eluted from SDS-PAGE. At page 23, Example 2-1, the specification merely states that the purified protein was electrophoresed in a SDS-PAGE to mainly show a single protein band with an IFN-γ inducing activity, which does not indicate that the protein after SDS-PAGE has the activity. As shown in the functional assays in Example 2-4, "a present purified protein" is used in the assays. In view of Example 1, which is directed to "preparation of purified protein", "a present purified protein" used in the functional assays demonstrated in Example 2-4 is purified using the procedure in Example 1, not from SDS-PAGE. Therefore, the "difference" between Nakamura's factor and the protein of the present invention in IFN-γ inducing activity of the protein after treatment on SDS-PAGE is not credible, and cannot be used to support the assertion that the two proteins are distinct.

Conclusion:

No claim is allowable.

Note: the record of the conclusion regards claim 97 has been confusing and ambiguous as it was allowed in some Office Actions, and not allowed in the others. Upon further reviewing the record of the prosecution history, the claim, and the prior art, the Examiner decides that claim 97 is not allowable, and it is rejected under 35 U.S.C. 103(a) for the reasons addressed above. The allowability of claim 97 in the previous Office Actions, which indicate that claim 97 is allowable, is withdraw.

Advisory Information:

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 703-305-1345. The examiner can normally be reached on Monday - Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER

Dong Jiang, Ph.D.
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AU1646
10/15/02